REMARKS

In response to the Office Action of April 7, 2004, Applicants have amended the claims, which, when considered with the following remarks, is deemed to place the present application in condition for allowance. Favorable consideration of all pending claims is respectfully requested.

In the April 7, 2004 Office Action, the Examiner rejected Claim 20 under 35 U.S.C.§ 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to he Examiner, the metes and bounds of the phrase "or other convenient means" are not clear.

In determining whether claims do, in fact, set out and circumscribe a particular area with a reasonable degree of precision and particularity, the definiteness of the language employed must not be analyzed in a vacuum, "but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art" *In Re Moore,* 439 F.2d 1232, 169 USPQ 236 (CCPA 1971).

Claim 20 is directed to the recombinant α-N-acetylglucosaminidase (NAG) according to claim 19 in pure form relative to non NAG material as determined by weight, activity, amino acid homology or similarity, antibody reactivity or other convenient means. In respect to "or other convenient means", the specification clearly sets out on page 30 and in Examples 7 and 8, the preferred methods for the preparation of and purification of recombinant NAG. One skilled in the art at the time the application

was filed would have understood that in addition to measuring purity by weight, activity, amino acid homology, similarity, or antibody reactivity, other well-known convenient means existed in the prior art for determining purity of recombinant NAG relative to non recombinant NAG.

Thus, Claim 20 is therefore sufficiently clear and definite as to comply with the requirements for definiteness under the second paragraph of 35 U.S.C. §112. Withdrawal of the rejection of Claim 20 under 35 U.S.C. §112, second paragraph is therefore respectfully requested.

The Examiner has rejected Claims 19-28, 30-31, 35-36, 60, and 62-66 under 35 U.S.C. §112, first paragraph, as allegedly directed to non-enabled subject matter. According to the Examiner, the specification does not reasonably provide enablement for an NAG isolated from any or all sources and having an amino acid sequence identity of 80% with that of SEQ ID NO:2 including mutants and variants and pharmaceutical compositions comprising the above enzymes. As presently amended, independent Claims 19, 35 and 60 no longer recite "an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth in SEQ ID NO: 2 ". Withdrawal of the rejection of claims 19-28, 30-31, 35-36, 60 and 62-66 under 35 U.S.C. § 112, first paragraph, is therefore warranted and respectfully requested.

Claims 19-31, 35-36 and 60-66 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly obvious over Sasaki et al. (1991) *J. Biochem. 110*(5): 842-846.

Sasaki et al. (1991) has been cited for teaching purification of a human NAG from human liver. The reference has also been cited for teaching that the enzyme is 80 kDa

when tested by SDS/PAGE and that a deficiency of the enzyme is known to cause MPS IIIB or Sanfilippo B syndrome, a severe neurodegenerative disease in humans.

The Examiner has taken the position that the enzyme disclosed in the reference and that claimed in the present invention are inherently one and the same and that Applicants have not done anything to the enzyme except to isolate the recombinant form of the purified enzyme disclosed in the reference.

Applicants respectfully traverse the rejection of claims 19-31, 35-36 and 60-66 under 35 USC § 102(b) and/or 35 USC § 103(a). It is respectfully submitted that the NAG described and claimed in the present application is distinguished from, and unobvious in view of, the NAG of the prior art in ways other than merely the fact that it is produced recombinantly.

With respect to the rejection of claims 19-31, 35-36 and 60-66 under 35 U.S.C. § 102(b), as allegedly anticipated by Sasaki et al. (1991), the Examiner has taken the position that the enzyme disclosed therein and that claimed in the present invention are inherently the same. "Since the enzyme has been isolated from a source identical to that in the instant application, Examiner also takes the position that the glycosylation aspect, molecular weight and the amino acid sequence the nucleotide sequence which encodes the enzyme are all inherent characteristics and the enzyme disclosed in the reference and that claimed are one and the same." Office Action, page 7.

In the first instance, Applicants would like to clarify that Sasaki et al. (1991) disclose NAG isolated and purified from human liver. In contrast, the present application teaches isolation and purification of NAG from human placenta (Example I), as well as isolation of a partial NAG cDNA from a blood leukocyte cDNA library, and isolation of

the remaining NAG coding sequence from a corresponding genomic clone, isolated by hybridization to a human chromosome 17 library (Example 4). The present application further teaches transfection of an NAG expression vector into cells, followed by purification of the recombinant enzyme. Thus, there does not appear to be an "identical source" shared by the disclosure of Sasaki et al. (1991) and the present application.

Further, Sasaki et al. "does not disclose the amino acid sequence of Applicants' claimed enzyme or the nucleotide sequence encoding the enzyme as capable of hybridizing to SEQ ID NO:1 or 3 under high stringency conditions" as the Examiner readily admits. *See* page 7, second paragraph of Office Action. A reference does not "describe" an invention within 35 U.S.C.§ 102, and thus is not an anticipation, unless that single reference contains sufficient disclosure to put the invention in the hands of the public. *See In re Outtrup,* 531 F.2d 1055, 189 USPQ 345 (CCPA 1976); *in re Coker* 463 F.2d 1344, 175 USPQ 26 (CCPA 1972); *In re Sheppard*, 339 F.2d 238, 144 USPQ 42 (CCPA 1964); *In re Brown*, 329 F.2d 1006, 141 USPQ 245 (CCPA 1964).

Thus, a claimed invention is not anticipated by a prior art reference if the alleged anticipatory disclosures cited as prior art are non-enabled. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.* 314 F. 3d 1313, 1354, 65 USPQ2d 1385, 1416 (Fed. Cir. 2003). Stated otherwise, in order to anticipate a claim, a reference must disclose every element of that claim and enable one skilled in the art to make the alleged anticipating subject matter." *PPG Industries, Inc. v. Guardian Industries Corp.,* 75 F3d 1558, 1566, 37 USPQ2d 1618, 1624 (Fed. Cir. 1996).

Since Sasaki et al. do not describe a single amino acid sequence of an NAG, nor a single nucleotide sequence encoding an NAG, the reference falls far short of enabling one skilled in the art to make the recombinant NAG recited in claims 19-31, 35-36 and 60-66.

Applicants further submit that the present application indicates that the molecular weights of the subject recombinant NAG are about 89 kDa and about 79 kDa, while the NAG purified from tissue sources has molecular weights of about 82 kDa and 77 kDa. *See* specification page 27, lines 6 to 16. The Examiner is directed to Weber et al. (2001) "Expression and Characterization of Human Recombinant –N- Acetylglucosaminidase" *Protein Expression and Purification* 21:251-259, a copy provided herewith at Exhibit A. The Weber et al. (2001) article confirms the molecular weights of the recombinant form of the enzyme. *See* p. 255, column 1. Accordingly, the presently claimed recombinant NAG is distinguished from the tissue-derived source of NAG disclosed by Sasaki et al (1991).

In view of the amendments to the claims and the foregoing remarks, withdrawal of the rejection of claims 19-31, 35-36, 60-66 under 35 U.S.C.§ 102(b) is respectfully requested.

With respect to the rejection of claims 19-31, 35-36 and 60-66 as obvious in view of Sasaki et al. (1991), the Examiner has stated that Sasaki et al. (1991) "not only provides a purified NAG enzyme but also identifies the role the enzyme plays in the inherited disease known as mucupolysaccharidosis IIB." Office Action, page 8. The Examiner has alleged, using the purified enzyme provided in Sasaki et al. (1991), that it would have been obvious to those skilled in the art to obtain its amino acid information by amino acid sequencing, isolate a cDNA clone from a cDNA library and the

recombinant form of the enzyme, or use a fusion protein fused to an affinity tag and express the protein in any of the host cells including insect cells or CHO cells using the isolated cDNA in a vector "as is well known in the art." *See* Office Action, page 8.

Applicants respectfully submit that the Examiner has engaged in improper hindsight reconstruction in making the obviousness determination. Both suggestion and reasonable expectation of success must be found in the prior art, not applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 492, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

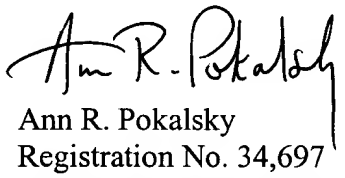
Sasaki et al.do not disclose a nucleotide sequence for an NAG cDNA, a recombinant NAG protein, or even an amino acid sequence for NAG. In providing a tissue-derived NAG enzyme, Sasaki et al. (1991) in its best light, can only be cited for providing an invitation to experiment. However, "obvious to try" is not the standard of 35 U.S.C. § 103. *In re Fine*, 837 F.2d 1071, 5 USPQ 2d 1596 (Fed. Cir. 1988).

Further, Applicants respectfully submit that the Examiner has not properly alleged the obviousness of the claimed products, but rather has alleged the obviousness of the methods by which the products might be made. In a rejection of product or composition claims for obviousness, the issue is "the obviousness of the claimed compositions, not of the method by which they are made." *See In re Deuel*, 51 F.3d 1552, 34 USPQ2d 12101 (Fed. Cir. 1995); *In re Bell*, 991 F.2d 781, 26 USPQ 1529 (Fed. Cir. 1993). Since Sasaki et al. (1991) provide absolutely no nucleotide or amino acid sequence information for an NAG enzyme, the presently claimed NAG cannot be obvious. Well known methods of amino acid sequencing or cDNA library screening such as those alluded to by the Examiner on page 8 of the Office Action, do not ameliorate the deficiency of teachings provided by Sasaki et al (1991).

Thus, it is apparent that the tissue-derived, purified enzyme provided by Sasaki et al. (1991) was not enough to suggest that one skilled in the art could produce the presently claimed recombinantly produced NAG with a reasonable expectation of success. Sasaki et al. (1991), provide no amino acid or nucleotide sequence information, which information proved critical in obtaining the presently claimed invention. *See* Examples 3-5, including Table 4, of the present application. Absent the knowledge of NAG protein sequence and both probe and primer design based on such sequence generation, there would have been no reasonable expectation of success in achieving the enzyme of the present invention. Withdrawal of the rejection of claims 19-31, 35-36, 60-66 under 35 U.S.C.§ 103(a) is therefore warranted.

In view of the foregoing remarks and amended claims, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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